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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,057	02/03/2004	Gregory E. Conner	03194-1-001200	1518

35596 7590 02/02/2009

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EXAMINER	
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ART UNIT	PAPER NUMBER
1616	
MAIL DATE	DELIVERY MODE
02/02/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/771,057	CONNER, GREGORY E.	
	Examiner	Art Unit	
	JAMES H. ALSTRUM ACEVEDO	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 November 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-11,18 and 21-28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-11,18 and 21-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-2, 4-11, 18-19, and 21-28 are pending. Applicants previously cancelled claims 3, 12-17, and 20. Applicants have amended claims 5, 11, and 19. Applicants amended claim set and remarks/arguments submitted on November 17, 2008 are acknowledged. All rejections not explicitly maintained in the instant office action have been withdrawn per Applicants' claim amendments. Applicants' claim amendments have necessitated a new rejection under § 103(a).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-11, 18, and 21-26 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

An analysis based upon the Wands factors is set forth below.

To be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without undue experimentation. In *Genentech Inc. v. Novo Nordisk* 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997); *In re Wright* 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993),. See also *Amgen Inc. v. Chugai Pharm. Co*., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir. 1991); *In re*

Fisher 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). Further, in *In re Wands* 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court stated:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman (230 USPQ 546, 547 (Bd Pat App Int 1986)). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims.

Breadth of Claims

Applicants' claims are broad with regards to the amount and concentration of hydrogen peroxide administered to the respiratory system of a mammal (clam 10 and claims dependent therefrom) or a primate (claims 1 and 11 and claims dependent therefrom). Applicants' independent method claims are broad with regards to the condition being treated in a patient exhibiting symptoms of cystic fibrosis (claim 1) or the lung infection being treated (claim 10), and thus include all lung conditions possible in patients with cystic fibrosis as well as any kind of infection (i.e. viral, fungal, bacterial, or parasitic).

Nature of the invention/State of the Prior Art

Applicants' invention is drawn to methods of treating lung conditions and/or lung infections in mammals, especially primates, exhibiting symptoms of cystic fibrosis, by administration of hydrogen peroxide optionally in combination with antifungal and antiviral agents. Some of Applicants embodiments require the coadministration of thiocyanate. Thiocyanate is an anion, thus, the recitation of thiocyanate in Applicants' claims is considered generic to any thiocyanate salt, because anions cannot stably exist in the absence of a suitable

cationic counterion to yield a charge neutral ionic compound. Applicants' claims require no specific amount of hydrogen peroxide or thiocyanate anion. It is noted that instant claims 9 and 18 only require a specific concentration of hydrogen peroxide as one of two possible alternative limitations.

An online Material Safety Data Sheet (MSDS-1) (accessed on July 10, 2008 at http://www.bu.edu/cs/labsafety/ESMSDSs/MSHydPeroxide.html) teaches that 30% w/w hydrogen peroxide (aq) is harmful when inhaled, causing chemical burns to the respiratory tract; may cause irritation to the respiratory tract with burning pain to the nose and throat, coughing, wheezing, and shortness of breath. The MSDS also teaches that inhalation of 30% hydrogen peroxide may also cause ulceration of nasal tissue, insomnia, nervous tremors with numb extremities, chemical pneumonia, **unconsciousness, and *death***. The MSDS (MSDS-2) (accessed on July 10, 2008 at http://www.jtbaker/msds/englishhtml/h4070.htm) for 3% aqueous hydrogen peroxide solution teaches that inhalation of a 3% aqueous hydrogen peroxide solution is not expected to be a health hazard under normal conditions and that inhalation of a 3% aqueous hydrogen peroxide solution is not expected to require first aid measures. MSDS-2 does not specify what are "normal conditions" nor under what circumstances first aid measures might be required upon inhalation of a 3 % aqueous hydrogen peroxide solution. The medical literature has recognized some cases of serious side effects or even fatal poisoning resulting from the non-accidental or accidental ingestion of 3% aqueous hydrogen peroxide (Ashdown et al. "Hydrogen Peroxide Poisoning: Causing Brain Infarction: Neuroimaging Findings," A.J.R. June 1998, 170, pp 1653-1655, especially pg. 1655, 1st sentence of discussion section). Watt et al. ("Hydrogen peroxide poisoning," Toxicol. Rev. 2004, 23(1), Abstract only) teach that almost most

inhalational exposure [to hydrogen peroxide] causes little more than coughing and transient dyspnea (i.e. difficult or painful breathing), but highly concentrated solutions of hydrogen peroxide can cause severe irritation and inflammation. Shock, coma, and convulsions may ensue and pulmonary edema may occur up to 24-72 hours post exposure (ibid). See also an online excerpt from "International Programme on Chemical Safety Poisons Information Monograph 946: Chemical", sections 2.2, 5.2, and 9.1.2 (accessed July 11, 2008 at http://www.inchem.org/documents/pims/chemical/pim946.htm).

The MSDS (MSDS-3) (accessed on July 10, 2008 at http://www.jtbaker/msds/englishhtml/p6181.htm) teaches that **inhalation of potassium thiocyanate causes irritation to the respiratory tract**, with symptoms including coughing and shortness of breath. The probable lethal dose of potassium thiocyanate is 15-30 grams.

Regarding infections, it is not logical that one can prevent an infection that is already present, such as Applicant claims in alternative limitations recited in claims 23 and 26. The art recognizes that the lactoperoxidase system (LPO system), which is based on the conversion of hydrogen peroxide and thiocyanate by a lactoperoxidase into the antibiotic $OSCN^-$ anion is effective against *Pseudomonas* (various species), *Staphylococcus aureus, Escherichia coli, Streptococcus* (various species), *H. influenzae, Bacillus cereus, and B. cepacia* [(1) Wijkstrom-Frei et al. "Lactoperoxidase and Human Airway Host Defense," Am. J. Respir. Cell Mol. Biol. 2003, 29, pp 206-212, especially pp 210-211; and (2) Conner et al. "The Lactoperoxidase system links anion transport to host defense in cystic fibrosis," FEBS letters 2007, 581, pp 271-278, especially pg. 272]. The art also recognizes that the LPO system is present in ovine and human airways [(1) Wijkstrom-Frei, ibid, abstract and (2) Conner et al., ibid, pp 271]. Conner et al.

acknowledges that continuous production of hydrogen peroxide and transport of thiocyanate (i.e. SCN^-) in the presence of LPO in vivo may not be able to eradicate an established infection (pp 276, right column, 1st full paragraph). Conner's data in Figure 3 on pg. 274 indicates that **addition of LPO or hydrogen peroxide in the absence of added SCN^- to washes from cultured secretions from cystic fibrosis (CF) lungs was unable to restore antibacterial activity in CF cultures** and only non-CF cultures showed antibacterial activity upon addition of LPO or hydrogen peroxide. Conner speculates that defects in SCN^- transport in cystic fibrosis (CF) patients may be an additional defect in the CF airway host defense and supports the need for further studies of SCN^- levels in CF airways (pp 277, last two sentences prior to the acknowledgements). Wijkstrom-Frei teaches that **the efficacy of the LPO antibacterial activity is known to depend on concentration of hydrogen peroxide, thiocyanate, and bacteria** (pg. 210, left column). Wijkstrom-Frei states that **the exact concentration of hydrogen peroxide in airway surface liquid (i.e. in the lung fluid) is unknown and is estimated to range from 10^{-6} to 10^{-4} M** (pp 211, 1st full paragraph in left column).

Level of One of Ordinary Skill & Predictability/Unpredictability in the Art

The level of a person of ordinary skill in the art is high, with ordinary artisans having advanced medical and/or scientific degrees (e.g. M.D., Ph.D., Pharm. D. or combinations thereof). There is a general lack of predictability in the pharmaceutical art. *In re Fisher*, 427, F. 2d 833, 166, USPQ 18 (CCPA 1970).

Guidance/Working Examples

Applicant's specification provides no guidance about what specific concentration of hydrogen peroxide is effective, but merely states that the amount administered results in a lung fluid concentration between 10^{-7} M and 10^{-4} M (see page 5, lines 4-7 of Applicant's specification). Similarly, Applicant's specification provides no guidance with regards to the amount of thiocyanate when administered is effective to treat a lung condition in primates exhibiting signs of cystic fibrosis or to treat lung infections in a mammal, but merely states that the amount administered results in a lung fluid concentration between about 5 micromolar and 4 mM (see page 4, lines 10-15 of Applicant's specification). Thus, an ordinary skilled artisan would be forced to rely on undue experimentation to discover the therapeutically effective ranges in the amounts and concentrations of both hydrogen peroxide and thiocyanate (e.g. potassium thiocyanate).

In conclusion, Applicant's specification is not enabling for the use of the claimed methods of treatment, as set forth above.

Response to Arguments

Applicant's arguments filed 11/17/08 have been fully considered but they are not persuasive. Applicants concede that their claims are broad and traverse the instant enablement rejection is improper by arguing that (1) Applicants' specification provides ample guidance by indicating the desired lung fluid concentration of hydrogen peroxide; (2) the exposure of the lungs to hydrogen peroxide levels of 3% is allegedly safe and Applicants' claimed ranges are several orders of magnitude lower; (3) the specification allegedly discloses therapeutically

effective amounts of thiocyanate that are to be administered; (4) the citation form the Conner FEBS Letters article (vol. 581, pgs 271 and 274 and Figure 3) are allegedly out of context; (5) the in vitro data allegedly does not show unpredictability; (6) there is allegedly no unpredictability in the identification of dose ranges and formulations; and (7) the delivery of medications via inhalers is well known in the art.

The Examiner respectfully disagrees with Applicants' traversal arguments. Regarding (7), the Examiner agrees with Applicants that the administration of medicaments via inhalation, in general, is well known in the prior art. However, it is noted that Applicants' claims do not require inhalation administration. The phrase "administering to the respiratory system" includes indirect methods of administering drugs to the lungs such as oral or intravenous methods, which result in systemic administration of drugs. Systemic administration would eventually administer drugs to the lungs as blood passes by the lungs and exchanges materials with the lungs via the alveoli. Nonetheless, the fact that it is known in the art that drugs may be administered by inhalation administration does not cure the deficiency in Applicants' specification of the specific amounts of hydrogen peroxide and thiocyanate that are necessary to obtain the desired results of lung fluid concentration of hydrogen peroxide of 10^{-7} M and 10^{-4} M. It is also noted that Applicants' claims and Applicants' specification does not define what constitutes a therapeutically effective amount of thiocyanate.

Arguments (5)-(6) are unpersuasive, because Applicants are alleging that pharmacokinetic and pharmacodynamic data are essentially predictive. Whereas Applicants have identified the concentrations of hydrogen peroxide (see paragraph [0010]) and thiocyanate (see paragraph [0008] in Applicants' specification) that they would like to obtain in the lung

fluid as a result of administering these compounds to the respiratory system, Applicants provide no guidance regarding the amounts of these compounds that when administered result in the desired lung fluid concentrations. It would require undue experimentation to ascertain what amounts of hydrogen peroxide and thiocyanate that when administered to the respiratory system result in the desired lung fluid concentrations of these compounds, because both hydrogen peroxide and thiocyanate are known to cause irritation to the lungs upon inhalation and both can result in death if given in the wrong amounts. Hydrogen peroxide administered at the wrong concentration can also cause death. Hydrogen peroxide is also recognized as being a reactive oxygen species that contributes to acute lung injury and tissue inflammation (See Kim et al. Exp. Mol. Med. 2008, 40(3), pp 320-31 (abstract only)). It is also known that that hydrogen peroxide induces significant increases in mitogen-activated protein kinases that result in cell death (Pelaia et al. J. Cell Biochem 2004, 93(1), pp 142-152 (abstract only)). The art also recognizes that inhaled oxidants (e.g. hydrogen peroxide) initiate a variety of pathological processes, including inflammation, which contributes to the pathogenesis and/or exacerbation of airways disease (Ciencewicki et al. Journal of Allergy and Clinical Immunology, 2008, 122(3), pp 456-468 [see pages 1, 10 [Figure 1], 20-22 of print out]). The art also recognizes the existence of a great variability in responses to inhaled oxidants, such as hydrogen peroxides, between different patient populations and in the same patient at different periods of said patient's life (Id. at pages 2 and 20-26). There is no guidance in Applicants' specification about differences in dosage amounts for patients of different ages or health. Based on the above, it is clear that the determination of dosage amounts is not predictable given the scant guidance provided by

Applicants that is limited to the desired result of the claimed method of achieving particular lung fluid concentrations.

Regarding (4), Applicant's assert that the in vitro data in Figure 3 shows limitations of the in vitro system used for testing and that this is not an indicator of unpredictability. The Examiner respectfully disagrees, because the limitations of the in vitro testing model point to the model's unreliability as a predictor of in vivo efficacy. Applicant's argument is also unpersuasive in light of the in vivo data (i.e. various MSDS cited on the record) demonstrating the serious damage or death that may result from the administration of hydrogen peroxide and thiocyanate. Clearly, the administration of substances likely to cause death or injury at the very least suggests the unpredictability of the in vivo efficacy based solely on the in vitro data. It is also noted that hydrogen peroxide has been shown to induce pathogenic increases in inflammatory mediators (e.g. Il-8) that results in cell death (Pelaia).

Argument (3) is incorrect. The specification in paragraph [0008] does not disclose therapeutically effective amounts of thiocyanate, but rather the desired result of the administration of therapeutically effective amounts of thiocyanate (i.e. a lung fluid concentration between about 5 micromolar and 4 millimolar). Identifying the result one would like to achieve upon administering an effective amount of thiocyanate fails to identify what is the effective amount of thiocyanate needed to achieve the desired result. This is not guidance, but a suggestion to the public to try to figure out what an effective amount might be. To meet the requirements of 112, 1st the specification must teach the ordinary skilled artisan how to make and use. Merely leading the ordinary skilled artisan to the point where it is obvious to try does not satisfy the requirements of 112, 1st. *In re Gardner*, 166 USPQ 138 (C.C.P.A. 1970).

Argument (2) appears to ignore the fact that there are literature reports of 3% aqueous hydrogen peroxide causing serious side effects or even fatal poisoning from both the accidental and non-accidental ingestion of 3% hydrogen peroxide (See Ashdown cited on page 5 of the office action mailed July 17, 2008).

Regarding (1), identifying the desired result or outcome does not provide enablement to the ordinary skilled artisan to arrive at the desired result/outcome without relying upon unduly burdensome experimentation to determine the dosages of hydrogen peroxide and thiocyanate that do not cause death, irritation of the respiratory tract, cell death, etc. An ordinary skilled artisan would also be required to study various patient populations (e.g. neonates vs. children vs. adults vs. elderly) to determine safe and effective dosages for these patient populations as well. To meet the requirements of 112, 1st the specification must teach the ordinary skilled artisan how to make and use. Merely leading the ordinary skilled artisan to the point where it is obvious to try does not satisfy the requirements of 112, 1st. *In re Gardner*, 166 USPQ 138 (C.C.P.A. 1970). The additional references cited above have only been cited to address Applicants' arguments. Thus, Applicant's specification does not enable the claimed method treating lung conditions and/or lung infections in mammals, including primates, absent undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9, 18, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 9, 18, and 27 are vague and indefinite, because each of these claims recites an alternative limitation requiring the administration of hydrogen peroxide "in an amount between 10^{-7} M and 10^{-4} M in the lung fluid" Molarity (i.e. M) is a unit of measurement indicating a concentration. Concentrations are not indicative of an amount. Thus, it is unclear how much hydrogen peroxide is administered. Furthermore, claim 27 recites in item b about the claimed inhaler, "administers hydrogen peroxide in an amount between 10-7 M and 10-4M in the lung fluid." This phrase does not communicate the amount of hydrogen peroxide administered by the inhaler, but merely states a desired result of the hydrogen peroxide administered. Thus, claim 27 does not communicate any unambiguous information about the amount of hydrogen peroxide administered. Appropriate correction and clarification are required.

Response to Arguments

Applicant's arguments filed 11/17/08 have been fully considered but they are not persuasive. Applicants argue that the phrase ""in an amount between 10^{-7} M and 10^{-4} M in the lung fluid", which is utilized to describe the amount of hydrogen peroxide is not ambiguous, because the use of concentrations in pharmaceutical patents is common place. This is unpersuasive, because it does not address the merits of the rejection above that the phrase "in an amount between 10^{-7} M and 10^{-4} M in the lung fluid" renders the cited claims indefinite. The phrase, "in an amount between 10^{-7} M and 10^{-4} M in the lung fluid," renders the rejected claims indefinite because it does not indicate the amount of hydrogen peroxide administered, but rather the desired result of the unspecified amount of hydrogen peroxide that is administered. Thus, it

would be unclear to an ordinary skilled artisan what amount of hydrogen peroxide is administered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 19-20 and 27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lin et al. (U.S. Patent No. 6,589,481).

Applicant Claims

Applicants claim an inhaler comprising (a) aerosolized hydrogen peroxide, (b) a peroxidase, or (c) thiocyanate (claim 19), which (i) administers an amount of hydrogen peroxide to the respiratory system of a mammal to decrease microbial load, (ii) administers hydrogen peroxide in an amount between 10-7 M and 10-4 M in the lung fluid, or (iii) further comprises an antibiotic, an anti-fungal, or an anti-viral (claim 27), or which comprises (a) hydrogen peroxide, (b) a peroxidase, or (c) thiocyanate and hydrogen peroxide (claim 28).

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

Lin teaches an apparatus to pretreat and sterilize a lumen device, which in some embodiments **the generator of the mist or aerosol comprises a liquid spray nozzle, a tank containing a liquid comprising hydrogen peroxide with a gas nozzle situated at least partially in** the liquid or a nebulizer (col. 3, lines 3-6). The generator of the aerosol comprising a liquid spray nozzle, a tank containing liquid comprising hydrogen peroxide with a gas nozzle situated at least partially in the liquid, reads on an inhaler. The minimal requirement of Applicants' rejected claims is an inhaler comprising hydrogen peroxide, because items (a), (b), and (c) in claims 19 and 27-28 or all written in the alternative. The intended use of items (a) and (b) of claim 27 is given little patentable weight. Furthermore, claims 19 ands 27-28 do not specify the amount of hydrogen peroxide contained in the inhaler nor its concentration. Thus,

any amount of hydrogen peroxide that could be administered from the inhaler must be reasonably expected to decrease microbial load if administered to the respiratory system of a mammal. It is the Examiner's position that upon use of the aerosol generator taught by Lin one would necessarily obtain an inhaler comprising aerosolized hydrogen peroxide.

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Lin lacks the express teaching of an inhaler comprising aerosolized hydrogen peroxide. This deficiency is cured by the teachings of Lin as explained below.

Finding of Prima Facie Obviousness Rationale and Motivation (MPEP §2142-2143)

It would have been prima facie obvious that upon use of Lin's aerosol generator containing liquid hydrogen peroxide that Lin's aerosol generator would comprise a finite amount of aerosolized hydrogen peroxide. It is a reasonable assumption that an aerosol generator containing liquid hydrogen peroxide connected to a gas nozzle would necessarily produce aerosolized hydrogen peroxide that would be contained within the aerosolized generator for at least a finite period of time, thus resulting in an inhaler comprising aerosolized hydrogen peroxide. Regarding claim 20, it would have been prima facie obvious to include an additional anti-bacterial or other anti-microbial agent, because sterilization is the process by which a device or surface is rendered devoid of microbes and Lin's invented apparatus accomplishes this by applying anti-bacterial hydrogen peroxide. The combination of It is generally considered *prima facie* obvious to combine two compounds each of which is taught by the prior art to be

useful for the same purpose, in order to form a composition which is to be used for the very same purpose. The idea for combining them flows logically from their having been used individually in the prior art. See *In re Kerkhoven*, 626, F.2d 848, 205 USPQ 1069 (CCPA 1980). Instant claim 20 defines nothing more than the concomitant use of two known sterilizing agents (i.e. hydrogen peroxide in combination with an additional anti-bacterial, anti-viral, or anti-fungal compound). It would follow that the recited claims define *prima facie* obvious subject matter. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 4-11, 18, and 20-26 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-17 of U.S. Patent No. 6,702,998 (USPN '998) for the reasons of record restated herein.

Although the conflicting claims are not identical, they are not patentably distinct from each other because they are substantially overlapping in scope and mutually obvious. Independent claims 1 and 10 of the instant application, claim methods of treating a lung condition (claim 1) or a lung infection (claim 10) in a primate exhibiting signs of cystic fibrosis (claim 1) or a lung infection in a mammal (claim 10) by administering an effective amount of hydrogen peroxide. Independent claims 1 and 10 of USPN '998 claim a method of treating a lung infection in a primate suffering from cystic fibrosis (claim 1) or a mammal (claim 10) by administration of aerosolized thiocyanate. Dependent claims 5 and 15 of USPN '998 indicate that hydrogen peroxide can be also be administered with the aerosolized thiocyanate in the methods of independent claims 1 and 10. Both USPN '998 and the instant application recite methods of treating lung infections (i.e. lung conditions) in primates (i.e. mammals) suffering from cystic fibrosis comprising administration of thiocyanate, a peroxidase, and/or hydrogen peroxide. The specific infective bacteria listed in claim 21 of the instant application are also recited in claims 3 and 12 of USPN '998. Both the instant application and USPN '998 also recite the combination of other treatments including breathing exercises, postural drainage, chest percussion, vibration, or assisted coughing. Importantly, claims 5 and 14 of USPN '998 claim a method of treating a lung infection in a primate suffering from cystic fibrosis (claim 5) or treating a lung infection in a mammal (claim 14) that further comprises in one alternative the step of administering hydrogen peroxide. The difference between the cited independent claims of the

instant application and USPN '998 is that the claims of the instant application administer hydrogen peroxide and the claims of USPN '998 administer thiocyanate. It is noted that several of Applicant's claims suggest in alternative limitations the administration of other active agents (e.g. thiocyanate). Thus, as evidenced by claims 5 and 14 of USPN '998, the administration of hydrogen peroxide to treat a lung infection, which is a species of lung condition, in primates exhibiting symptoms of cystic fibrosis or mammals having a lung infection represents an obvious modification of the claims of USPN '998. Therefore the Examiner concludes that claims 1-2, 4-11, 18, and 21-26 are prima facie obvious variants of claims 1-17 of USPN '998.

Response to Arguments

Applicant did not traverse the instant rejection and has indicated that the rejection is premature. The Examiner respectfully disagrees, because the Examiner is required to make all rejections deemed to be proper under the various relevant statutes/rules. The above obviousness-type double patenting rejection is not a provisional rejection. Given Applicant's apparent agreement that the instant rejection is proper, the only means of overcoming the instant rejection are to (a) file a proper terminal disclaimer or (b) adequately amend the claims to distinguish the claimed inventions. The instant rejection is maintained.

Conclusion

Claims 1-2, 4-11, 18-19, and 21-28 are rejected. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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